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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,757	08/24/2001	Bettina Mockel	P 282664 000445 BT	8904

909 7590 03/23/2004

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EXAMINER	
KERR, KATHLEEN M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/935,757	MOCKEL ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,12,13,15,16,18 and 21-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,12,13,15,16,18 and 21-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-final rejection (mailed on October 6, 2003), Applicants filed a response and amendment received on January 6, 2004. Said amendment cancelled Claims 1-8, 10, 11, 14, 17, 19, 20, amended Claims 9, 12, 13, 15, 16, and 18, and added new Claims 21-28. Thus, Claims 9, 12, 13, 15, 16, 18, and 21-28 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the foreign applications 10043336.7 and 10126422.4 filed in Germany on September 2, 2000 and May 31, 2001, respectively. Applicants note in their remarks that translations of the priority documents would be forthcoming; no such documents have been received. Thus, the priority documents, in German, cannot be used to establish an earlier effective filing date for the claimed subject matter.

As previously noted, the instant application is granted the benefit of priority for the U.S. Provisional Application No. 60/295,009 filed on June 4, 2001; the subject matter of the pending claims is disclosed in the provisional application; thus, the effective filing date of the pending claims is June 4, 2001.

Withdrawn - Objections to the Specification

3. Previous objection to the specification because the title is not descriptive is withdrawn by virtue of Applicants' amendment.

4. Previous objection to the specification for lacking continuity data in the first paragraph is withdrawn by virtue of Applicant's amendment.

5. Previous objection to the specification for the order of its content is withdrawn by virtue of Applicants' amendment.

6. Previous objection to the specification for being confusing on page 6, line 20, with the phrase "enzyme sigma factor E" is withdrawn by virtue of Applicants' amendment.

Maintained - Objections to the Specification

7. Previous objection to the Abstract is maintained/amended herein. While Applicant's amendment inserted the necessary source species as requested by the Examiner, the amended Abstract is in an improper format. The Abstract should be a single, narrative paragraph (see M.P.E.P. § 608.01(b)). Correction is required.

Withdrawn - Objections to the Claims

8. Previous objection to Claims 15 and 16 for having improper structure of a Markush group is withdrawn by virtue of Applicants' amendment.

9. Previous objection to Claim 18 for being drawn to non-elected subject matter is withdrawn by virtue of Applicants' amendment.

10. Previous objection to Claim 18 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicants' amendment.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

11. Previous rejection of Claims 9-16 and 18 under 35 U.S.C. § 112, second paragraph, as being indefinite for the metes and bounds of "**the** sigE gene of nucleotide sequences which code for it" is withdrawn by virtue of Applicant's amendment to cite specific sequence of the sigE gene.

12. Previous rejection of Claims 9-16 and 18 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "in particular overexpressed" is withdrawn by virtue of Applicants' amendment.

13. Previous rejection of Claims 10, 11, and 18 under 35 U.S.C. § 112, second paragraph, as being indefinite for the terms "biosynthesis pathway" and "metabolic pathways" is withdrawn by virtue of Applicants' cancellation and/or amendment of said claims to remove these terms.

14. Previous rejection of Claims 14 and 18 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "regulatory properties of the polypeptide (enzyme protein) for

which the polynucleotide sigE codes" is withdrawn by virtue of Applicants' cancellation and/or amendment of said claims to remove this term.

15. Previous rejection of Claims 15, 16, and 18 under 35 U.S.C. § 112, second paragraph, as being indefinite for the structure of "15.1, 15.2" is withdrawn by virtue of Applicants' amendment.

16. Previous rejection of Claims 15 and 18 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "codes for lysine export" is withdrawn by virtue of Applicants' amendment.

17. Previous rejection of Claims 9-16 and 18 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicants' amendment to specify the structure of the sigE gene in all the pending claims.

18. Previous rejection of Claims 9-16 and 18 under 35 U.S.C. § 112, first paragraph, scope of enablement, is withdrawn by virtue of Applicants' amendment.

19. Previous rejection of Claim 14 under 35 U.S.C. § 112, first paragraph, enablement, is withdrawn by virtue of Applicants' cancellation of said claim.

20. Previous rejection of Claim 15 under 35 U.S.C. § 112, first paragraph, scope of enablement, is withdrawn by virtue of Applicants' amendment deleting specific reference to feedback resistance genes.

Maintained - Claim Rejections - 35 U.S.C. § 112

21. Previous rejection of Claims 15 and 16 under 35 U.S.C. § 112, second paragraph, as being indefinite for the metes and bounds of phrases like "**the** dapA gene" (emphasis added) maintained/amended. Although the claims have been amended, the following question remains as previously presented:

> "The article "the" in many of the claims indicates a single gene, but which gene? Only one example of each of the listed genes, all from *C. glutamicum*, is described in the instant specification (see pages 12-14). Must the dapA gene that is enhanced be the endogenous *Corynebacterium* dapA gene of the cell claimed (if the cell is *C. glutamicum*, must enhancement be of a C. *glutamicum* dapA gene or can a dapA gene from *C. melassecola* be added to meet the limitations of the claim)?" (emphasis added).

Thus, while the cell used in the method is limited to *C. glutamicum*, the "one or more genes" is not required to be from *C. glutamicum*. Thus, the article "the", referring to a single species, is unclear. Clarification is required.

Also in Claims 15 and 16, various genes are noted. The inclusion of both the gene name (or abbreviation) and the enzyme name is confusing. For example, if a gene for glucose-6-phosphate dehydrogenase was named gpd and not "zwf" as required in the claims, would this read on the claim or not? Many genes are incorrectly identified during genome projects and the like, thus using gene names to identify any gene encoding a particular enzyme is confusing. The Examiner suggests removal of the gene name limitation entirely.

Also in Claims 15 and 16, the nature of the following proteins is unclear: "a protein for lysine export", "a Zwa1 protein", and "a Zwa2 protein". These proteins are unclear as to their metes and bounds from simply their name or their function. While the specification gives references for specific examples of these proteins, no limitation to these specific proteins can be

read into the claims. Thus, one of skill in the art would unclear as to the genus of genes encoding a protein for lysine export, for example. Clarification is required.

Withdrawn - Claim Rejections - 35 U.S.C. § 102

22. Previous rejection of Claims 9, 12, 13, and 18 under 35 U.S.C. § 102(b) as being anticipated by Kimura *et al*. (EP 0864654) is withdrawn by virtue of Applicants' amendment.

NEW ISSUES

Objections to the Specification

23. The amendment filed January 6, 2004 is objected to under 35 U.S.C. § 132 because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: in the first paragraph, the incorporation of 60/295,009 by reference is improper unless said application is an exact duplicate of the instant application, wherein such incorporation is redundant.

Applicant is required to cancel the new matter in the reply to this Office Action or to explain how this incorporation by reference is not new matter citing clear support in the specification as originally filed for the entire application of 60/295,009.

24. The amendment filed January 6, 2004 is objected to under 35 U.S.C. § 132 because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall

introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: inserting the "RNA polymerase" into the description of sigma factor E on page 6.

Applicant is required to cancel the new matter in the reply to this Office Action or to explain how this insertion is supported in the specification as originally filed.

The Examiner notes that this amendment was in direct response to an objection to the specification concerning the clarity of "enzyme sigma factor E" in the specification. To delete the phrase "RNA polymerase" (in response to this objection) and maintain clarity of the specification, Applicants must comment on the skill of the art concerning sigma factor E – how this protein is not an "enzyme" and how this protein, when named sigma factor E, is clearly part of the genus of well-known proteins in the art to be associated with RNA polymerase functionality.

Claim Objections

25. Claim 22 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 9 already requires the full-length of SEQ ID NO:1 to be "overexpressed". Thus, the limiting to a smaller portion of SEQ ID NO:1 in Claim 22 does not further limit the claimed subject matter.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

26. Claims 9, 12, 13, 15, 16, 18, and 21-22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 9, the inclusion of the description of the gene as SEQ ID NO:1 AND encoding SEQ ID NO:2 is confusing, particularly in light of the definition of overexpression in the specification on page 10 (which definition is addressed in an enablement rejection below). Clarification is required.

27. Claims 9, 12, 13, 15, 16, 18, and 21-22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 9, item b, it is unclear what is being used to "enrich"? The cells will grow without assistance upon culturing as is clear by the well-known definition in the art of "culturing". The Examiner suggests deleting step b entirely.

28. Claim 15 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. To clearly define the group, the Examiner suggests inserting ---following--- before "group" as the language of Claim 16 is written. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

29. Claims 15-16 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 25-26 are drawn to a method optionally using genes for proteins by name only wherein said gene is claimed solely by function and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held as described above. While genes encoding known enzymes with particular functions, such as genes encoding dihydrodipicolinate synthase, are adequately described by virtue of their specification function and their examples in the art, this is not the case for genes encoding proteins without clear support in the art for their genus: a protein for lysine export, Zwa1 protein, and Zwa2 protein. The mere name of these proteins does NOT connote a structure and/or function as is the case with the specific enzymes noted elsewhere in the claims. One example of each is noted in the specification; however, no description of how to maintain Zwa1-like protein structure and/or function is found. Thus, one of skill in the art would be unable to predict the structure of other members of the genus of genes claimed.

30. Claims 9, 12, 15, 16, 18, 21-28 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for overexpressing SEQ ID NO:1

by transforming a host cell with a vector comprising SEQ ID NO:1 and a promoter wherein the promoter is responsible for the overexpression, does not reasonably provide enablement for overexpressing SEQ ID NO:1 by means otherwise mentioned in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To practice the claimed invention to the full extent of its scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

In the specification on page 10, means of overexpression are described. Said means include not only increasing the copy number of a gene or regulating the gene with a particular promoter, which means are enabled by the art, but also include altering the ribosome binding site, altering the lifetime of the mRNA, altering the protein so as to prevent degradation, and altering media conditions, all of which are known in the art to "overexpress" a gene in specific examples, but none of which are predictable with sigE or other genes that lack specific examples in the art. The specification provides no working examples or direction for overexpression using means of ribosome binding site, altering the lifetime of the mRNA, altering the protein so as to prevent degradation, and altering media conditions. The nature of the invention is that these means are specific to a particular gene sequence and cannot be extrapolated from other, unrelated genes; there is no particular recipe of media that will overexpress all genes. Thus, overexpression using these methods is wholly unpredictable and not enabled by the specification or the art.

Claims 12, 23, and 26 are included in the instant rejection because the use of the vector and/or promoter does not limit the concept of "overexpression". Claim 15 also has enablement issues of overexpressing the additional genes. Claim 13 is free of this rejection because of the specificity of the means of overexpression in the claims.

31. Claims 15-16 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known zwa1, zwa2, and lysC genes as described in the specification, does not reasonably provide enablement for methods using other of these genes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate

in scope with these claims. To practice the claimed invention to the full extent of its scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized above.

The instant specification teaches particular examples of lysC, zwa1, and zwa2 from the art. The art fully enables using these particular genes. While the instant specification describes and enables means for identifying other lysC, zwa1, and zwa2 genes using hybridization methods, etc., these methods do not enable one of skill in the art to make all, or a relevant portion of, the polynucleotides within the scope of the claims because the ability to find a lysC, zwa1, and zwa2 gene, which is structurally related said sequences, is not equivalent to the ability to make a lysC, zwa1, and zwa2 genes as required by the statute (i.e., "make and use"). No description in the specification or the art provides particular residues whose encoding is important within the disclosed sequence so that its lysC-, zwa1-, and zwa2-nature is maintained. Thus, one of skill in the art would be unable to predict the structure of the other members of the genus in order to make such members. Therefore, the instant claims are not enabled to the full extent of their scope.

Summary of Pending Issues

32. The following is a summary of the issues pending in the instant application:

a) The Abstract stands objected to for having an improper format.
b) The amendment filed January 6, 2004 stands objected to under 35 U.S.C. § 132 because it introduces new matter into the disclosure – for both an incorporation by reference statement and for the insertion of "RNA polymerase" into the specification.
c) Claim 22 stands objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

d) Claims 9, 12, 13, 15, 16, 18, and 21-22 stand rejected under 35 U.S.C. § 112, second paragraph, for both redundant phrasing in Claim 9, item a, and for the overall clarity of step b in Claim 9.
e) Claims 15 and 16 stand rejected under 35 U.S.C. § 112, second paragraph, for the metes and bounds of phrases like "**the** dapA gene".
f) Claim 15 stands rejected under 35 U.S.C. § 112, second paragraph, for omitting "following".
g) Claims 15-16 stand rejected under 35 U.S.C. § 112, first paragraph, written description, for the names of the genes used, which are not limited to those described in the specification as from *C. glutamic*um.
h) Claims 9, 12, 15, 16, 18, 21-28 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, for means of overexpression as elaborated in the specification on page 10.
i) Claims 15-16 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, for methods using other zwa1, zwa2, and lysC than those described in the specification.

Conclusion

33. Claims 9, 12, 13, 15, 16, 18, and 21-28 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution. The instant Office action is NON-FINAL due to the newly presented rejections concerning overexpression in light of the specification, in particular.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr
Examiner
Art Unit 1652

March 18, 2004